



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-N-2039]

Development of Best Practices in Physiologically Based Pharmacokinetic Modeling To Support Clinical Pharmacology Regulatory Decision-Making; Public Workshop

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop.

SUMMARY: The Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER), in collaboration with the Center for Biologics Evaluation and Research (CBER), is announcing a public workshop entitled “Development of Best Practices in Physiologically Based Pharmacokinetic Modeling to Support Clinical Pharmacology Regulatory Decision-Making.” The purpose of this public workshop is to discuss best practices and evidentiary criteria in the use of physiologically based pharmacokinetic (PBPK) modeling approaches to support regulatory decision-making; share experiences and cases where applying PBPK modeling and simulation highlight the opportunities and limitations of this approach; obtain input from stakeholders on when, where, how, and with what limitations PBPK modeling and simulation may be applied in regulatory decision-making; and discuss the knowledge gaps and research needed to advance PBPK modeling sciences in drug development to support regulatory decisions. This public workshop is also being conducted to satisfy one of FDA’s performance goals included in the sixth reauthorization of the Prescription Drug User Fee Amendments (PDUFA VI), part of the FDA Reauthorization Act of 2017 (FDARA), to hold a series of workshops related to model-informed drug development (MIDD).

DATES: The public workshop will be held on November 18, 2019, from 8 a.m. to 5 p.m., Eastern Time. See the SUPPLEMENTARY INFORMATION section for registration date and information.

ADDRESSES: The public workshop will be held at FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503, B and C), Silver Spring, MD 20993-0002. Entrance for public workshop participants (non-FDA employees) is through Building 1 where routine security procedures will be performed. For parking and security information, please refer to:

<http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.)

FOR FURTHER INFORMATION CONTACT: Lauren Milligan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3159, Silver Spring, MD 20993-0002, 240-402-6421, email: Lauren.Brum@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Under FDARA, and in accordance with section I, part J of the PDUFA VI Performance Goals, FDA agreed to convene a series of workshops to identify best practices for MIDD (<https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf> at 27). FDA is conducting this workshop as part of the MIDD workshop series.

PBPK modeling is a drug development tool that mathematically integrates physiological, physicochemical, and drug-dependent preclinical and clinical information to predict an investigational drug's absorption, distribution, metabolism, excretion, and pharmacokinetics (PK). Over the past several decades, there has been extensive research using PBPK modeling

and simulation to address a wide range of clinical questions, such as exploring the effects of extrinsic factors (e.g., concomitant medications, food intake) and intrinsic factors (e.g., age, organ dysfunction, disease status, genetics) on drug exposures.

FDA notes that PBPK modeling and simulation approaches are extensively used in regulatory submissions to predict the potential for drug-drug interactions and to support dosing recommendations for certain drugs when they are co-administered with metabolic enzyme modulators. However, challenges and knowledge gaps prevent PBPK modeling from being routinely used for specific regulatory decisions. Given the current limitations of the approach, it is important that the scientific community explore when, where, and how PBPK modeling and simulation may be applied in regulatory decision-making.

II. Objectives

The objectives of the workshop are to:

1. Discuss “best practices” in integrating in vitro and in vivo data to develop PBPK models and developing evidentiary criteria for PBPK models to be used for regulatory decision-making
2. Share experiences and cases applying PBPK modeling and simulation that highlight the opportunities and limitations of this approach
3. Obtain input from the stakeholders on when, where, how, and with what limitations PBPK modeling and simulation may be applied in regulatory decision-making
4. Discuss the knowledge gaps and research needs to advance PBPK modeling sciences in drug development and regulatory evaluation

A detailed agenda will be posted in advance of the workshop at <https://www.fda.gov/Drugs/NewsEvents/ucm633778.htm>.

III. Participating in the Public Workshop

Registration: Persons interested in attending this public workshop must register online by November 8, 2019, at <https://www.eventbrite.com/e/pbpbk-modeling-to-support-clinical-pharmacology-regulatory-decision-making-tickets-59005519096>. Please provide complete contact information for each attendee.

Registration is free and based on space availability, with priority given to early registrants. Early registration is recommended because seating is limited. FDA may limit the number of participants from each organization. Registrants will receive confirmation when they have been accepted. If time and space permit, onsite registration on the day of the public workshop will be provided beginning at 8 a.m.

If you need special accommodations due to a disability, please contact Lauren Milligan (see FOR FURTHER INFORMATION CONTACT) no later than November 8, 2019.

Streaming Webcast of the Public Workshop: This public workshop will also be webcast. A live webcast of this workshop will be available at <https://www.fda.gov/Drugs/NewsEvents/ucm633778.htm> on the day of the workshop. If you have never attended a Connect Pro event before, test your connection at https://collaboration.fda.gov/common/help/en/support/meeting_test.htm. To get a quick overview of the Connect Pro program, visit https://www.adobe.com/go/connectpro_overview. FDA has verified the website addresses in this document, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

Transcripts: Please be advised that as soon as a transcript of the public workshop is available, it will be accessible at <https://www.fda.gov/Drugs/NewsEvents/ucm633778.htm>. It may be viewed at the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. A link to the transcript will be available on the internet at <https://www.fda.gov/Drugs/NewsEvents/ucm633778.htm>.

Dated: June 6, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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